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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/413,109	10/06/99	ZHANG W	INRP:087/SHS

HM12/0908

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EXAMINER	
GUZO,D	
ART UNIT	**PAPER NUMBER**
1636	5

DATE MAILED: 09/08/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/413,109	Zhang et al.
Examiner	**Group Art Unit**
David Guzo	1636

☒ Responsive to communication(s) filed on *Oct 6, 1999*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *22-97* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *22-97* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

Applicants' request that the computer readable form of the Sequence Listing filed in the parent application 08/145,826 be used to prepare a file for the instant case is acknowledged. A Sequence Listing for this application will be prepared.

New claims submitted in preliminary amendments filed 10/6/99 and 12/21/99 have been renumbered as **claims 22-97** as per the requirements of 37 CFR 1.126.

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 22-97 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating cancers comprising administration of the Ad5CMV-p53 recombinant adenovirus, does not reasonably provide enablement for treating any cancers comprising using any adenovirus comprising the p53 gene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with the information known in the art without undue experimentation (United States v. Teletronics Inc. 8 USPQ2d 1217 (Fed. Cir. 1988). Whether undue experimentation is needed is not based upon a single factor, but rather a

conclusion reached by weighing many factors. These factors are outlined in *Ex parte Forman* 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988) and they include the following:

1) Unpredictability of the art. The gene therapy art is extremely unpredictable. Often the ability of a vector to express a therapeutic transgene in cells *in vivo* is dependent upon the specific vector chosen, the vector design, the promoter used to derive expression of the transgene, the method of delivering the vector to the target cells, etc. (See Fox, Nature Biotechnology, 2000, Vol. 18, pp. 143-144; Kmiec, American Scientist, 1999, Vol. 87, pp. 240-147; Anderson, Nature, 1998, Vol. 392, pp. 25-30; Verma et al., Nature, 1997, Vol. 389, pp. 239-242; Ross et al., Human Gene Therapy, 1996, Vol. 7, pp. 1781-1790, etc.). Given the unpredictable behavior of gene therapy vectors *in vivo* and given the many failures in gene therapy, it is impossible to predict, *a priori*, the *in vivo* characteristics of gene therapy vectors and whether said vectors will have any therapeutic effects in patients.

2) State of the art. The state of the art at the time of applicants' invention was nil with no examples of successful treatment of human cancers using adenoviral (or any other) vectors.

3) Amount of guidance provided by applicants. The only vector exemplified in the instant specification and the only vector which possesses the recited *in vivo* activities is the Ad5CMV-p53 vector. The Ad5CMV-p53 vector is a "first generation" adenoviral vector containing a deletion of the E1a and E1b regions and substitution of an expression cassette for said deleted region. However, the claims encompass second generation adenoviral vectors which are not

disclosed in the specification (i.e. no working examples are described), wherein the procedures which would be used to generate said vectors are not disclosed (i.e. what packaging cell lines would be necessary to package these vectors, what procedures would be used to delete portions of the E3, E4, etc. genes, what portions of the E3, E4, E2, etc. genes would need to be deleted, etc.). Applicants' specification provides no guidance on how the skilled artisan would generate these second generation adenoviral vectors and only recites that other adenoviral genes can be deleted and serve as potential insertion sites for expression cassettes. These teachings are essential for practicing the claimed invention and must be included in the specification. Assertions that the skilled artisan would have been able to provide the missing teachings cannot compensate for a lack of an enabling disclosure (See *Genentech v. Novo Nordisk A/S*, 42 USPQ2d 1000, 1997).

4) Number of working examples. Applicants' only working example is the Ad5CMV-p53 vector.

5) Scope of the invention. The invention is broad with the claims reading on use of any adenoviral vector comprising the p53 gene inserted at any genomic location and under the control of any promoter to treat any cancer in humans.

6) Nature of the invention. The invention involves one of the most complex and unpredictable aspects of molecular biology/medicine; gene therapy using recombinant viral (adenoviral) vectors.

7) Level of skill in the art. The level of skill in the gene therapy art is high; however, as noted by some of the most prominent gene therapy researchers (i.e. W. French Anderson, Verma, etc.), the level of unpredictability in this poorly developed art is high.

Given the above analysis of the factors which the courts have determined are critical in ascertaining whether a claimed invention is enabled, it must be considered that the skilled artisan would have had to have conducted undue and excessive experimentation in order to practice the claimed invention.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 22-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 9-13, 22-52 and 56-72 of copending Application No. 08/459,713 (hereafter the '713 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant application and the 713 application recite the same methods for treating human cancer patients comprising administering pharmaceutical compositions comprising adenoviral vectors containing the p53 gene. The claims in the '713 application differ in that they recite adenoviral vectors comprising expression cassettes for expression of the p53 gene (i.e. use of the CMV IE1

promoter, SV40 early polyA signal) wherein said expression cassettes are encompassed within the claims in the instant application, were disclosed in the '713 application and could have been claimed in the '713 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 22-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 30-35 of copending Application No. 08/626,678 (hereafter the '678 application). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '678 application recite pharmaceutical compositions comprising recombinant adenoviral vectors capable of expressing the p53 gene, wherein said pharmaceutical compositions are designed to be administered to humans for treatment of cancer (as per the instant claims). It would have been obvious to the ordinary skilled artisan to use the pharmaceutical compositions claimed in the '678 application in methods of treating cancer since these adenoviral vectors are specifically designed to express a tumor suppressor gene (p53) which inhibit tumorigenicity or cause the death of cancer cells. With regard to the expression cassettes used to drive expression of the p53 gene in the adenoviral vectors, said expression cassettes are encompassed within the claims in the instant application, were disclosed in the '713 application and could have been claimed in the '678 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, George Elliott, can be reached on (703) 308-4003. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
September 6, 2000

DAVID GUZO
PRIMARY EXAMINER